Major Cancer Biology

within the Master Program 'Molecular Biosciences' University of Heidelberg, Faculty of Biosciences



The Major Cancer Biology teaching activities are published here:

Heidelberg University system heiCO (preliminary public view: https://tinyurl.com/heiCO-DKFZ)

Major Cancer Biology website: <u>https://www.dkfz.de/en/major-cancer-biology/StudyProgram/StudyProgram-Alt.2.html</u> (visible to the public)

Major Cancer Biology Sharepoint: https://webcoop.dkfz-heidelberg.de/sites/major-cb (accessible to current students and teachers)

Overview: HP-L's offered in WS2024/2025 – Modules "Biolab" and "Working in Bioscience"

<u>Definition:</u> A 'Biolab' or 'Working in Bioscience' lab internship – duration: minimum 6 weeks in the lab (extensible) – should consist of a small scientific project. The experimental work must be recorded by a protocol report which has to be written in the style of a master thesis, consisting of title page, abstract, introduction, materials and methods, results, discussion and references.

"Biolab"(only for MolBio students with Major Cancer Biology) – "Working in Bioscience" (also for MolBio-Students from other Majors) – additional options: "for students from other Heidelberg Master programs: _____program name _____" / "and for other interested students" (external, Erasmus

exchanges, etc.)

"Leistungsnachweis/Mode of Examination": standard for Major Cancer Biology students to fulfill Module Biolab:

The experimental work has to be recorded and the protocol report will be graded by the instructor on a scale from 0 - 100 points.

In addition, the supervisor may request that the experimental work is presented in a lab meeting seminar.

lfd Nr.	Term University calendar	Туре	Supervisor(s)Contact	 Duration and date Time Location No. of places 	Title and Description
1.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major: MCB) also for Master Molecular Biotechnology also for Master Translational Medical Research 	 Amir Abdollahi and co-workers a.amir@dkfz.de 	 to be arranged 9:00-18:00 HIT-INF450 and NCT-INF460 2 	Tumor microenvironment, radiation oncology and translational cancer research The main focus of our lab is to investigate the role of tumor-stroma communication in development of tumor resistance to multimodal therapies and rational design of novel therapy strategies. For a recent overview please read: Abdollahi and Folkman. Evading tumor evasion: Current concepts and perspectives of anti-angiogenic cancer therapy. Drug Resist Updat. 2010 (download @ http://angiogenesis.dkfz.de/papers/abdollahi_drugresist_2010.pdf). We seek for candidates with an excellent scientific record and strong motivation in multidisciplinary projects. Solid background in basic cell and molecular biology techniques are requested. Experiences in the field of tumor angiogenesis and tumor microenvironment, radiation biology, genome/transcriptome and epigenetic analysis (microarrays based mRNA, miRNA, SNP, CGH and promoter methylation studies), analysis of large data sets generated with high- throughput methods (basic statistics, R, SQL), functional genomics (RNAi or pharmacological in- vitro and in-vivo screens), proteomics (expression, purification, phosphorylation and protein- protein interaction analysis) are favourable and the focus of our laboratory. Special skills with animal experimentation, including transgenic mouse models, surgical orthotopic tumor implantation, intravital microscopy or other invasive or non-invasive imaging tools (MRI, CT-scan, PET and ultrasound) are advantageous for the evaluation of the applicant. Our team is integrated in Heidelberg Ion Therapy Center and National Center for Tumor diseases (NCT) which offer state-of-the-art research facilities and a supportive multidisciplinary environment. For more information about our group please visit: <u>www.molecularoncology.de</u>

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2.	all-year offer collective heiCO # 8503WPM 100	• X Biolab for Major Cancer Biology students only	 Hellmut Augustin and co-workers h.augustin@dkfz.de sandra.schneider@dkfz.de 	 to be arranged 8.00-18.00 DKFZ, INF 280, 4. floor 1-2 	Methods in angiogenesis research The term angiogenesis describes the growth of new blood vessels from existing vessels. This process is responsible for essential biological functions such as embryonic development, the female reproductive cycle, wound healing and tissue repair processes. Pathological conditions in which angiogenesis is active are malignant neoplasm/tumor and additional diseases such cardiovascular diseases, diabetes, multiple sclerosis or autoimmune disorders. The aim of the underlying course is to provide an overview of endothelial cell biology and to gain experience in several standard angiogenesis assays.
3.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major: Infectious Diseases) 	 Stella Autenrieth stella.autenrieth@dkfz.de 	 6-8 weeks; date to be arranged 8:00-18:00 DKFZ, ATV, A2.206 1 	Dendritic Cells in Infection and Cancer Host defense against microbial pathogens and cancer relies on the concerted action of both innate and antigen-specific adaptive immunity. Key features of the innate immune system include the ability to rapidly recognize pathogens or malignant cells and to signal these events to cells of the adaptive immune system. Dendritic cells (DCs) are critical for defense against infection and cancer. They are unique antigen-presenting cells that are able to recognize and respond to pathogens and inflammation by, among others, contributing to the initiation and regulation of T- cell responses. Our research group focuses on the questions which factors impair the development of DCs in bacterial infections or in patients with multiple myeloma and what are the consequences for the immune response. Moreover, we are interested in biomarker discovery on blood immune cells to predict therapy response using spectral flow cytometry. More information on https://www.dkfz.de/en/virus-assoziierte-karzinogenese/groups/AGAutenrieth
4.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: Infectious Diseases, Systems Biology and other interested students 	 Marco Binder m.binder@dkfz.de 	 longer-term internship, duration and dates to be arranged 8:00-18:00 DKFZ, ATV, A2.212 1-2 	Virus replication dynamics and the innate antiviral response of cells My research group investigates the very early events upon virus infection. We focus on both, the virus- particularly the dynamics of its very initial replication, as well as on the host cell. A particular interest of my group is the intracellular recognition of virus infection and the induction of the intrinsic antiviral response, an important and ubiquitous branch of the innate immune system. Dysregulation of these responses either leads to susceptibility to fulminant viral replication and/or chronification of the infection, or to exacerbated and/or chronic inflammation. We apply methods of molecular and cell biology, biochemistry but also systems biology. More information on http://www.dkfz.de/en/virus-assoziierte-karzinogenese/groups/AGBinder
5.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Jan Gerwin, Kim Boonekamp m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Image-based phenotypic data analysis Image-based high-throughput screening serves as a powerful tool in both fundamental and translational research. We are making use of colorectal cancer organoids to further dissect cancer signaling pathways and to detect cancer dependencies possibly leading to the identification of novel drug targets. The combination of these patient avatars with various signaling pathway reporters that are introduced via genetic engineering enables to study drug sensitivity in general or drug effects on specific pathways. In the context of this project, we are generating large image-based datasets. We offer opportunities to participate in designing and running image analysis pipelines using bioinformatic approaches with a focus on the programming language R. This project allows students to expand on their bioinformatic skills and work with large datasets based on phenotypic data in the context of cancer. Reference: Betge et al., Nat Com. 2022

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6.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Jan Gleixner m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Bioinformatics Functional genomic approaches such as cell-based screens generate very large data sets that need to be computationally analyzed. The experimental approaches to gain functional insights include RNA interference (RNAi) and genome editing (CRISPR/Cas9) techniques. We offer opportunities to participate in exciting software projects in the context of design, analysis and storage of large-scale data. This will support interested students to further expand their knowledge of modern programming languages such as R, Python, Perl or JavaScript as well as cutting edge technologies in the field of web development. <u>References:</u> Rauscher et al, Molecular Systems Biology, 2018; Rauscher, Heigwer et al, Nucleic Acids Res., 2017; Heigwer et al., Genome Biology, 2016; Winter et al., Bioinformatics, 2015
7.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Florian Heigwer, Javed Iqbal m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Artificial Intelligence & High-Performance Computing for Organoid Analysis 3D image-based screening for cancer organoids allows more precise phenotypical analysis and visualization of cancer cells. However, the computational costs involved in the analysis of 3D images are very high. We are developing scalable, secure, robust, and efficient methods to orchestrate analyses in cloud applications and thereby reduce the computational costs involved in analyzing high-dimensional images. Within this project, students are given the opportunity to learn the intricate details of deep- learning based 2D and 3D microscopy image segmentation and computational feature extraction. They will be introduced to basic and advanced concepts of machine learning in the context of image-based profiling of perturbation screens of an organoid platform. This computational project involves cloud application development and data analysis using various programming languages such as R, Python, Julia, Rust, CUDA and WebJS. <u>References:</u> Heigwer et al., Methods Mol Biol., 2021; Scheeder et al., Current Opinion in Syst. Biol., 2018; Heigwer et al., Cell Systems, 2023
8.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Pradhipa K. Manivannan Martina Zowada m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Image-based high-throughput phenotypic screening Automated high-throughput phenotypic screening is a powerful approach used to assess and quantify intricate morphological characteristics, including shape, size or texture, in cellular models or organisms. This technique allows to investigate the effects of chemical or genetic perturbations by compound library treatments and CRISPR/Cas9 or RNAi, respectively. By capturing and analyzing a multitude of morphological features, this screening method enables the rapid identification of compounds or genetic factors that induce specific phenotypic changes. Phenotypic screening can be used to delineate a drug's mode of action by comparing drug-specific phenotypic responses, thereby being of high relevance in the early stages of drug discovery. Phenotypic screening is also widely used in functional genomics studies to identify gene functions and dissect complex biological pathways. In this project, we use state-of-the-art methods for phenotypic screening in cell line as well as organoid models of cancer, focusing on the latest advancements in the field. This project provides students with a comprehensive understanding of how large-scale high-throughput chemical and genetic screens are conducted in 2D and 3D cell culture models including cell culture work as well as the use of robotics, automated microscopy, and liquid handling technologies. References: Scheeder et al., Curr Opin Syst Biol. 2018; Heigwer et al., Cell Syst 2023

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9.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Fillip Port m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Precision genome engineering to model cancer genetics <i>in vivo</i> Novel CRISPR modalities such as base- and prime editing can install defined sequence changes with high purity in multicellular organisms. We use such tools to induce known or suspected cancer mutations in selected cell types and monitor the resulting phenotypes in vivo. In this practical you will use the model organism <i>Drosophila melanogaster</i> to induce and test cancer mutations in the context of an intact organism. The short generation time of <i>Drosophila</i> means that you can go from hypothesis to result in the course of a single lab rotation, allowing you to perform your own mini project in the lab. Techniques will include advanced genome engineering, molecular biology, genetics with a tractable model organism and high-resolution microscopy. <u>References:</u> Doll et al., Sci Adv, 2022; Port et al., PNAS 2020; Port et al., eLife 2020; Port and Bullock, Nature Methods, 2016; Port et al., PNAS, 2014
10.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Siamak Redhai m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Combining single cell RNA-seq with CRISPR perturbations to build genetic networks CRISPR-Cas has revolutionized genomic research and with the recent development of single cell RNA-sequencing, we can begin to understand how mutations effect the transcriptome of individual cells. We are looking for a highly motivated individual who has experience in molecular biology techniques (e.g PCR, primer design, knowledge in sc-RNA-seq ect) to facilitate our already existing pipeline in order to identify CRISPR mutations in single cells. This is a great opportunity to learn state-of-the-art techniques and gain knowledge on how CRISPR in combination with sc- RNA-seq can be used to build genetic networks. <u>References:</u> Redhai et al., 2020 Nature; Port et al., 2020, eLife; Bahuguna et al., 2021
11.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Siamak Redhai, Shivohum Bahuguna m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Understanding Wnt signaling using cell biology in the Drosophila intestine Wnt signaling is an evolutionary conserved signaling cascade that is involved in developmental and pathological processes. With such diverse roles, understanding how this pathway is regulated at the cell biological level, e.g via endosomes and lysosomes, is currently of great interest to the scientific community. We primarily use the Drosophila intestine as our model organ since it has diverse cell types, including stem cells, and is amendable to genetic manipulations. Using state-of-the-art technologies such as CRISPR, RNAi, high-resolution imaging, we aim to understand how organelles in intestinal cells regulate the activity of Wnt signaling and how this is changed in disease conditions. We offer multiple avenues for students to conduct research, including opportunities to translate findings in mammalian systems. <u>References:</u> Redhai et al., 2020 Nature; Port et al., 2020, eLife

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12.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Antonia Schubert, Nadine Winkler m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Signaling through extracellular vesicles Extracellular vesicles (EVs) are mediators of intercellular communication. Different EV populations can be distinguished by their size and cellular origin. EVs contain a variety of pathway-activating components and to some extent represent the parental cells. This project aims to contribute to a better understanding of vesicle-mediated signal transduction in cancer. A pathophysiological significance especially of Wnt signaling pathway components in and on EVs could be shown for various malignancies. Therefore, the mechanistic details of EV- mediated signaling pathway transduction will be investigated using Wnt signaling pathways as an example. For this purpose, EVs of benign and cancer cell lines, from patient-derived organoids and patient blood will be isolated and characterized. The students will get the opportunity to gain hands-on experience isolating EVs from different Sources according to good manufacturing practices. Additionally, they will apply the different EV fractions in various down-stream analyses, such as protein quantification, nano particle tracking, Western blot, electron microscopy, mass spectrometry, and luciferase reporter assays. <u>References:</u> Gross, Chaudhary et al., Nat. Cell Biology, 2012; Worst et al., Cancers, 2019; Schubert and Boutros, Mol. Oncology, 2021
13.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Boutros, Oksana Voloshanenko, Cornelia Redel, Kim Boonekamp, Saskia Reuter m.boutros@dkfz.de 	 to be arranged 9:00-18:00 INF 580 (TP3) 1 	Wnt signaling in cancer The Wnt signaling pathway is an evolutionarily conserved signal transduction pathway involved in processes such as animal development from Hydra to humans and homeostasis. Wnt signaling has been implicated in cancerogenesis and is often dysregulated in cancer with key genes being either mutated or overexpressed. In current projects we are dissecting the Wnt signaling pathway in developmental and pathological conditions. The aim of the projects will be to characterize the role of novel regulators possibly involved in canonical or non-canonical Wnt signaling, to analyze proteins which regulate Wnt secretion or to identify the roles of up-regulated Wnt ligands in colorectal cancer. The following techniques will be applied as part of the practical: gene editing by CRISPR/Cas9, gene silencing by siRNA, luciferase reporter systems, Western Blotting, 2D and 3D cell culture models including intestinal organoids and the option to set up new assays for novel genes of interest. References: Ambrosi et al., eLife 2022; Wolf et al., J Cell Sci, 2021; Voloshanenko et al., Science Reports, 2018; Voloshanenko et al., FASEB Journal, 2017; Voloshanenko et al., Nature Communications, 2013

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14.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: Infectious Diseases, Systems Biology) 	 Timo Bund, Ekaterina Nikitina, Kristina Alikhanyan, Sumen Munchol t.bund@dkfz.de 	• to be arranged • 9:00-18:00 • DKFZ IIC/ATV 0.206 • 1-2	 Bovine Meat and Milk Factors (BMMF) as drivers of indirect carcinogenesis The epidemiological link between the high consumption of bovine meat and milk products and the global incidence e.g. of breast and colorectal cancer (CRC) stimulated the search for a zoonotic infectious, carcinogenic agent. The division "Episomal-Persistent DNA in Cancer- and Chronic Diseases" headed by Dr. Timo Bund together with Prof. Harald zur Hausen isolated >100 different episomal, plasmid-like DNA agents from bovine meat and milk (therefore termed Bovine Meat and Milk Factors, BMMF) and peritumoral colon cancer tissue. BMMF are bioactive and replicate and transcribe/translate BMMF proteins in human cells. Our current hypothesis suggests an indirect role of BMMF in formation of specific types of cancer - as drivers of indirect carcinogenesis - in particular in colorectal cancer. We suggest that BMMF infection triggers chronic inflammation in the pre-cancerous tissues fueling radical formation and induction of DNA mutations in proliferative cells as precursors for cancer after several decades of BMMF latency. This project comprises immunohistochemical analysis of cancer tissue of different entities to monitor BMMF positivity and associations with host marker genes and cell populations. State-of-the-art multi-omics-analysis is used for identification of BMMF InA, and protein and interaction with the host including std. phenotypical readouts (like replication, viability, proliferation, cytotox, immune/antibody tests). BMMF isolated from the disease context will be re-engineered by molecular biological methods and applied on transfection Infection starling of BMMF activity in humans and might provide new measures for prevention of BMMF infection and cancer. References: zur Hausen H, Bund T, de Villiers EM. 2017. Infectious Agents in Bovine Red Meat and Milk and Their Potential Role in Cancer and Other Chronic Diseases. Curr Top Microbiol Immunol 407:83-1583.
15.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) 	 Maïwen Caudron-Herger m.caudron@Dkfz- Heidelberg.de 	 >=8 weeks; date to be arranged full-time DKFZ; INF 280, H1.03.064 1 	RNA-binding proteins in regulation of cell proliferation RNA and RNA-binding proteins (RBPs) are frequently deregulated in cancer, highlighting their druggable potential. Using the results of a screen that identified proteins that rely on RNA for interacting with other proteins (so-called RNA-dependent proteins), we identified a number of major mitotic factors as potential RNA-dependent proteins. Therefore, our aim is to understand how RNA-protein complexes involving mitotic factors impact cell division and govern cancer cell proliferation.

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16.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Priya Chudasama, Valentin Schmidt, and group members priya.chudasama@nct- heidelberg.de 	 to be arranged full-time DKFZ, TP4, INF 581 1-2 	Precision Sarcoma Research Sarcomas are a large and heterogeneous group of aggressive tumors arising from a variety of connective tissues such as muscles, fat, nerves, blood vessels and bone. These tumors have significant genetic and histologic diversity and variable clinical course, and metastatic sarcoma are largely incurable. Thus, there is an urgent need to develop more effective and less toxic therapies. In the Precision Sarcoma Research Group, we perform multi-level characterization genomic, epigenomic, transcriptomic landscapes of clinically annotated sarcomas to capture potentially clinically relevant molecular aberrations. We select promising candidates to perform functional and mechanistic validation using comprehensive employing state-of-the-art technologies. Prospective research projects would combine advanced molecular biology methods, functional genomics screens, high-throughput reporter assays, drug screens, microscopy as well as multi- omics data analysis and integration from sarcoma tumors and cell models to dissect molecular mechanisms regulating sarcomagenesis and target validation. Both wet-lab and dry-lab projects are envisioned. Major focus areas of our group include - Investigation of perturbed telomere maintenance mechanisms in sarcomas - Targeting sarcoma drivers using drug-induced protein degradation - Inquiry of the immune landscape of sarcomas to identify entry points for individualized immunotherapeutic approaches For details, please visit: <u>https://www.dkfz.de/en/praezisions-sarkomforschung/index.php</u>
17.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Angel Cid, Isaac Quirós a.cid@dkfz.de 	 to be arranged full-time DKFZ, HH, INF 280, H2.07.057 1-2 	Isolation of CD8 T cells reactive to tumor antigens: TCR identification and characterization Tumor-specific neoantigens arise from patient-specific mutations, most importantly in cancer- driving genes that are constitutively expressed by tumor cells, We are interested in the identification of neoantigen-reactive T cell receptors (TCRs) from the repertoire of patients and healthy individuals, which could be useful for cancer immunotherapy. The tasks include isolating CD8 T cells, followed by TCR cloning and testing of their capacity to recognize tumor cells and induce cytotoxic responses.
18.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 James Cleland, Duncan Odom james.cleland@dkfz.de 	 to be arranged 9:00-17:00 DKFZ, TP3, INF 580 1 	Mechanisms of sexual dimorphism in liver cancer The Odom lab at DKFZ is always searching for talented, motivated and collegial Master students to do rotation/thesis projects with us. We offer first-class training in cutting-edge experimental and/or computational genomics approaches (e.g. single cell/spatial transcriptomics), exciting projects on a wide range of topics both closely and loosely related to cancer, a fun and supportive working environment and personalised mentorship geared toward getting you to your desired next step in or out of academia. We are currently searching for a student to join our quest to understand sexual dimorphism in liver cancer. They will have the opportunity to choose from several possible rotation projects according to their biological/technical interests. Please reach out if you have questions! https://www.dkfz.de/en/regulatorische-genomik/index.php
19.	all-year offer collective heiCO # 8503WPM 100	• X Biolab • X WiB (also for Major: MCB)	 Tobias P. Dick t.dick@dkfz.de 	 to be arranged 9.00-18.00 DKFZ, INF 280, H2.02 1 	Redox regulation of signal transduction Please refer to our website for topics and references. http://www.dkfz.de/en/redoxregulation/inhalte/researchinterests/startres.html

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20.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: MCB, Systems Biology) and other interested students 	 Cihan Erkut, Claudia Scholl cihan.erkut@nct- heidelberg.de 	 to be arranged full-time DKFZ, TP4, INF 581 1 	Integrative genomics of rare cancers Our group studies rare and poorly-understood cancers with the aims to elucidate the underlying molecular mechanisms and discover new therapeutic entry points. Although they make up one out of five cancers in Europe, rare cancers are especially challenging to study due to the fact that relatively few patients for each cancer type are available. Our strategy to address this challenge is to augment laboratory experiments with thorough computational analysis of large "omics" (genomics, transcriptomics, proteomics, etc.) data. We integrate omics data from patient samples (mainly from the precision oncology program MASTER) and determine recurrent tumor-specific alterations (e.g, mutations, fusion genes, aberrant gene expression, etc.). These alterations are then functionally characterized in the laboratory, which involves hypothesis-driven omics experiments performed on cell lines and mouse models. We also perform large-scale CRISPR screening to uncover secondary gene dependencies. Finally, we expand our results with additional information from external datasets and curated knowledgebases. We offer small projects that focus on certain stages of these computational analyses as part of ongoing projects in the division. The practical will provide training in basic bioinformatics and data science. Experience with programming (R, Python), shell scripting, workflow management, handling large data and high-performance (cluster) computing would be an advantage.
21.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Aurélie Ernst a.ernst@dkfz.de 	 to be arranged 9.00-18.00 DKFZ, TP3, INF 580 1-2 	Genome instability Unknown before the next-generation sequencing era, chromothripsis is a recently discovered phenomenon of genome instability, by which a presumably single catastrophic event generates extensive genomic rearrangements of one or a few chromosome(s). Importantly, chromothripsis may initiate a substantial proportion of human cancer cases - as more cancer genomes are being sequenced, more and more tumor types are identified, for which chromothripsis plays a major role. In addition, chromothripsis is linked with poor prognosis for cancer patients. Our goal is to decipher the mechanistic basis of chromothripsis, the context in which it arises and the implications for cancer patients. Our lab applies a wide range of methods going from cell culture to CRISPR/Cas, immunofluorescence analysis and microscopy, single-cell genomics and mouse models. For further details, please visit our website: https://www.dkfz.de/en/genominstabilitaet-in-tumoren/index.php
22.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) 	 Marieke Essers m.essers@dkfz.de 	 to be arranged full-time DKFZ, INF 280, H01.04.058 1 	The bone marrow under inflammatory stress Hematopoietic stem cells (HSCs) and their bone marrow niche are under constant challenges. States of inflammation and infection in the bone marrow have been linked to irreversible changes in this microenvironment and the transformation of these stem cells. In the 'Inflammatory stress in stem cells' group we investigate the impact of inflammation and inflammatory signaling on the bone marrow in order to better understand the role in leukemia onset and progression. For this we combine mouse models, in vitro co-cultures and experiments with patient material to analyze the changes in cell composition and function using flow cytometry, gene expression analysis and imaging. PLEASE NOTE: This Biolab rotation will involve working with experimental mice. For further details of the work program and associated literature, please visit https://www.dkfz.de/en/aktivierung-haematopoetische-stammzellen/index.php Note: We also host long-term internships to guest and exchange students, please get in contact for individual arrangements.

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23.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major: MCB) 	 Aoife Gahlawat aoife.gahlawat@dkfz.de 	 No. or places to be arranged full-time NCT, INF 460 2 	Blood based biomarkers in Radiation Oncology Our group is interested in using patient blood as a source of "liquid biopsy" in patients who are undergoing radiotherapy. We are particularly interested in the role of the systemic immune system, using methods such as CyTOF for high dimensional phenotyping at the single-cell level and multiplex ELISAs. We are also investigating extracellular vesicles in radiotherapy, and their role in cell-cell communication. Taken together, we aim to identify biomarkers of radioresistance and disease response which can translate into the clinical setting. We are looking for highly motivated students who are open-minded and proactive.
24.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and MSc Molecular Biotechnology and other interested students 	Clarissa Gerhäuser c.gerhauser@dkfz.de	 to be arranged full-time DKFZ, Main Building, H2.03.070 1 	Using long-read nanopore sequencing to analyzing the interplay between somatic and structural variants and epigenetic alterations in prostate cancer Prostate cancer is a heterogeneous disease demonstrating distinct variations in their underlying molecular alterations, clinical features and therapeutic responses. Prostate cancer is characterized by frequent structural variations and few recurrent mutations in oncogenic driver genes. The interplay between structural and somatic variants and epigenomic events such as DNA methylation alterations in deregulating gene expression is poorly understood. This project will involve ONT long-read nanopore sequencing to analyze genomic and epigenomic alterations in human prostate cancer tissue and integrate the data with gene expression information to understand the multi-omic basis of prostate cancer heterogeneity. Localized relationships between DNA methylation, chromatin accessibility, mutations and structural variants and their role in deregulating gene expression will be investigated. The internship will involve both wet-lab techniques and bioinformatic investigations and should last a minimum of 12 weeks. Please also check our website at: https://www.dkfz.de/en/CanEpi/cancer_chemoprevention.html for further information on ongoing projects. <u>References:</u> 1. Sollier, E. et al., Bioinformatics (2024), 10.1093/bioinformatics/btae354 2. ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium, Nature (2020), 10.1038/s41586-020-1969-6 3. Gerhauser, C. et al. Cancer Cell (2018). 10.1016/j.ccell.2018.10.016 4. Weischenfeldt, J. et al. Cancer Cell (2013). doi: 10.1016/j.ccr.2013.01.002
25.	all-year offer collective heiCO # 8503WPM 100	• X Biolab for Major Cancer Biology students only	 Violaine Goidts, Emma Phillips v.goidts@dkfz.de 	 to be arranged full-time DKFZ, TP3, INF 580, 1.205 1 	Identifying new therapeutics against glioblastoma stem-like cells Glioblastoma is a highly lethal cancer for which novel therapeutics are urgently needed. Two distinct subtypes of glioblastoma stem-like cells (GSCs) were recently identified: mesenchymal and proneural. To identify mechanisms to target GSCs from one or the other subtype and thereby optimize potential therapeutic response, we combined transcriptomic expression analysis and kinome-wide short hairpin RNA screening of mesenchymal and proneural GSCs (Cheng et al., 2015). This project will involve characterisation of one of the candidate genes which is specific for the mesenchymal subtype. The methods involved in the project will include cell culture techniques, production of lentvirus, phenotypic assays to investigate invasion and clonogenicity, microscopy and irradiation studies. Please see our website for more information: http://www.dkfz.de/en/genetics/pages/projects/Glioblastoma_stem- like_cells/Glioblastoma_stem-like_cells.html

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26.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and MSc Molecular Biotechnology Master Translational Medical Research 	 Ed Green e.green@dkfz.de 	 to be arranged flexible DKFZ, Main Building, 6th floor 1-2 	Molecular biology - reducing bottlenecks in personalised therapeutics The manufacture of candidate personalised therapeutics (T cell receptors and antibodies) in the lab is time and cost intensive, limiting the application of these cutting edge therapies. We offer opportunities to participate in projects to determine what steps in our personalised therapeutics can be made more efficient. These range from standard molecular biology techniques (determining best bacterial strains and molar ratios of components), automation (programming liquid handling robots and connecting devices through open source drivers) and data driven design of DNA constructs (streamlining code, writing graphical interfaces). Depending on the project, strong molecular biology or programming skills (R/Python or others) would be an advantage.
27.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and MSc Molecular Biotechnology 	• Ed Green • e.green@dkfz.de	 to be arranged flexible DKFZ, Main Building, 6th floor 1-2 	MolBio / Bioinformatics: refining plasmid nanopore sequencing pipelines for synthetic biology Synthetic biology is integral to modern science, whether manufacturing therapeutic antibodies, gene reporter vectors, or plasmid libraries. Increasingly the limiting factor is not the cost of DNA synthesis, but the cost of sequencing material to ensure it is correct. NGS sequencing based on Illumina is expensive and slow: in contrast nanopore sequencing devices are cheap, easy to use, and provide long read data. Here we will refine plasmid sequencing pipelines, focussing on either the bioinformatic presentation of the results (e.g. improved tools, improved visualisation, improved speed, improved automation) or the molbio setup of reactions (testing different conditions to maximise efficiency, and attempting to miniaturise various steps to reduce costs). <u>References:</u> https://nanoporetech.com/sites/default/files/s3/literature/plasmid-sequencing-best-practice- workflow.pdf https://www.biorxiv.org/content/10.1101/2022.01.25.477550v1
28.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and MSc Molecular Biotechnology MSc Translational Medical Research and other interested students 	 Felix J. Hartmann felix.hartmann@dkfz.de 	 to be arranged full-time DKFZ, TP4, INF 581 1 	 Multiplexed Imaging and Single-Cell Analysis of Metabolic Interactions in the Tumormicroenvironment Progression and clinical outcomes of human cancer is influenced by cellular interactions in the tissuemicroenvironment (TME). We want to understand the spatial organization and cellular regulation of the human immune system and how they are influenced by tumor cells. To do so, we use a novel imaging platform termed MIBI (multiplexed ion beam imaging), which enables highly multiplexed (up to 40 dimensions) imaging of cell-specific protein expression and spatial localization in tissues. Research projects in our lab span different topics: 1) Systems Immunology: Comprehensive analysis of the human immune system directly from clinical samples to identify novel biomarkers. 2) Single-Cell Biology: We develop experimental tools to study novel aspects of cell biology on the single-cell level, e.g. the connection of cellular metabolism and epigenetic remodeling. 3) Computational biology: In collaboration with computational scientists, we apply novel approaches that utilize the singe-cell and subcellular nature of our datasets. Taken together, our vision is to advance our 78understanding of the interactions between the immunotherapeutic approaches in cancer and beyond.
29.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and MSc Molecular Biotechnology 	 Ilse Hofmann i.hofmann@dkfz.de 	 to be arranged full-time DKFZ, Main Building, first floor 1 	Antibodies as versatile tools to understand, diagnose and treat cancer You will learn how generate monoclonal and recombinant antibodies with an emphasis on screening design to obtain antibodies for the desired assay. Moreover, the student will learn how to validate antibody specificity and how to produce and purify antibodies.

lfd Nr	Term	Туре	 Supervisor(s) Contact 	Duration and date Time	Title and Description
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30.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major: MCB) and other interested students 	 Ilse Hofmann i.hofmann@dkfz.de 	 to be arranged full-time DKFZ, Main Building, first floor 1 	Cell adhesion and signaling in cancer Over the past decade, several studies on the subcellular distribution of p120-catenin family revealed that these proteins are not only constituents of cell-cell contact structures but also found dispersed in the cytoplasm and nucleus. Moreover, in their non-junctional form they are complexed with RNA-binding proteins and mRNA. This suggests that in addition to establishing and maintaining cell adhesive functions these proteins may also play roles in nuclear and ribonucleoprotein processing mechanisms. Our aim is to characterize the function of p120-catenin family members in these complexes and to discover how the exchange between the junctional and the non-junctional state is regulated. Moreover, the contribution to signaling cascades in healthy and malignant situations, e.g. cancer, will be evaluated. We apply methods of molecular and cell biology and also biochemistry. Please refer to our website for topics and references (<u>http://www.angiolab.de</u>)
31.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Ashok Kumar Jayavelu, Maithryen Kuppuswamy ak.jayavelu@dkfz.de 	 6-8 weeks; date to be arranged full-time OMZ, INF 350 EG2.224 1-2 	Deciphering non-genetic mechanisms governing cancer and drug response Cancer has long been thought of as a process governed by genetic factors. However, it is becoming more and more clear that non-genetic mechanisms can be just as essential. Principally, non-genetic mechanism such as cell signaling driven by cell extrinsic and cell intrinsic processes can lead to a variety of phenotypic states in cancer with distinct functional characteristics. Understanding the non-genetic molecular basis orchestrating cancer drug resistance phenotypes are our research focus. We utilize state-of-the-art high throughput and high sensitive mass spectrometry (MS)-based proteomic technologies as a discovery tool and combine with molecular approaches such as CRISPR to investigate the functional relevance. The course will offer hands on training in cell culture handling, sample preparation, LC-MS/MS, data analysis and visualization. This will be applied to one of the ongoing projects. Please find more info here: https://www.dkfz.de/en/paediatrische-leukaemie/Research-Group- Proteomics-and-Cancer-Cell-Signaling.html <u>References:</u> Jayavelu AK et al, 2020 Nature ; Jayavelu AK et al, 2022 Cancer Cell ; Bahrami E et al, 2023 Molecular Cancer
32.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) and MSc Molecular Biotechnology 	 Cindy Körner c.koerner@dkfz.de 	 to be arranged full-time DKFZ, TP3, INF 580, B2.302 1 	CRISPRa and prime editing for the study of regulatory promoter mutations in cancer Gene expression is tightly controlled by transcription factors binding to specific sequence motifs in gene promoters. Cancer has been described as a genetic disease and a variety of cancer- driving mutational events altering cellular gene expression patterns and behavior has been identified. In recent years, certain mutational events in promoter regions have been shown to contribute to cancer development. However, since these events are often non-recurrent, their impact to cancer progression has not been studied in detail, yet. We hypothesize that individual patients may carry individual mutations in promoter regions that contribute to cancer development and progression in a highly personalized manner by providing and alternative mechanism driving aberrant expression of proto-oncogenes. Hence, identification of these mutations might improve clinical disease management by taking into account the respective proto-oncogene as potential driver. We have developed a bioinformatic pipeline to annotate and characterize rare but potentially functional promoter mutations, which were then validated by promoter luciferase assay. The here proposed project would aim at the optimization of methods to study the functions of the promoter mutations and of the affected downstream target gene. Technically, this would include the use of molecular biology techniques to manipulate expression of the candidate gene (siRNA, CRISPR prime editing, CRISPRa) as well as phenotypic investigation of the consequences of manipulation. Hence, we invite applicants with a strong background in cell culture and basic molecular and cellular biology techniques.

lfd Nr	Term	Туре	 Supervisor(s) Contact 	 Duration and date Time Location No. of places 	Title and Description
33.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) and MSc Molecular Biotechnology 	 Cindy Körner c.koerner@dkfz.de 	 to be arranged full-time DKFZ, TP3, INF 580, B2.302 1 	Unraveling the functional consequences of 5'isomiRs in breast cancer Breast cancer is a heterogeneous disease which clinically presents with various subtypes varying in terms of treatment and prognosis. While the establishment of targeted therapeutics for some of these subtypes has strongly improved the clinical management of breast cancer, there are still many patients who cannot be treated successfully with current strategies. Therefore, there is the strong need to more deeply understand potential causes for differential therapy response and metastasis formation in patients of the same subtypes. In the recent past, the advent of high-throughput small RNA sequencing has enabled researchers to reconsider the dogma of one pre-miRNA giving rise to one or two distinct mature miRNA forms. Instead, alternative dicing or post-processing modifications generate a variety of so-called isomiRs for many miRNA species. Previous studies in our lab but also in other groups have revealed that such isomiRs are indeed expressed in breast cancer patient samples and that the target spectra and therefore also the phenotypes associated with canonical miRNAs and their 5'isomiRs can be entirely different from each other. Preliminary bioinformatics analysis indicates that the generation of certain isomiRs can be different between different patients posing two main questions: How is this regulated? What are the consequences of alternative miRNA processing? These questions can be addressed either from a bioinformatics or from a cell biology perspective. Therefore, we are interested to recruit highly interested and motivated students with a strong background in either of these fields. Bioinformatically, the project would involve the analysis and processing of large miRNA-seq datasets from both clinical and cell culture samples along with a variety of associated analyses of the clinical data of the patients and the sequence characteristics of the alternatively processed miRNAs. For a cell biology student, the project would consist of the
34.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: MCB, Neuroscience, Dev. Biol.) 	 Lena Kutscher and team I.kutscher@kitz-heidelberg.de 	 to be arranged full-time TP3, B4.208 2 	Neurodevelopmental principles underlying pediatric brain cancer Pediatric cancer is the leading cause of disease-related death in children, with central nervous system (CNS) tumors being the deadliest form. Unlike adult cancers, pediatric brain cancer is thought to arise from maturation blocks during brain development. Despite its impact on children's health, our understanding of the developmental underpinnings of pediatric brain cancer is limited. The Kutscher Lab investigates how germline and somatic alterations halt normal developmental trajectories to form (pre)malignant cells, using genetically engineered mouse models, human induced pluripotent stem cell (hiPSC) models, and single-cell RNA-seq of normal brains and tumor samples. We are broadly interested in the genetic and molecular mechanisms underlying developmental cell death, cerebellum cell type specification, and tumor initiation. We focus on medulloblastoma, a malignant embryonal tumor arising from the developing cerebellum. Given that pediatric cancer can be thought of as a disease arising from dysregulated development, understanding both normal developmental principles and how development is altered following mutations will be key to fully understand medulloblastoma formation. Please get into contact with Dr. Kutscher for details on specific projects. <u>https://www.dkfz.de/en/entwicklungsbiologische-urspruenge-paediatrischer-krebserkrankungen/index.php</u>

lfd Nr	Term	Туре	Supervisor(s)Contact	 Duration and date Time Location No. of places 	Title and Description
35.	all-year offer collective heiCO # 8503WPM 100	• ⊠ Biolab • ⊠ WiB (also for Majors: MCB, Systems Biology)	 Jeroen Krijgsveld j.krijgsveld@dkfz.de 	 to be arranged to be arranged DKFZ, TP4, INF 581, Rm S2.226 1 	Proteomics of stem cells and cancer Our main interest is to develop and apply proteomic approaches to understand how dynamic regulation of the proteome underlies processes that are fundamental to cancer and stem cells, primarily focusing on cell signaling and chromatin regulation. We mainly work with high-end mass spectrometric technologies, and combine this with innovative biochemical approaches to investigate protein expression, interaction and secretion in various cellular systems. The practical course will provide training in the use of mass spectrometry for protein identification and quantification, involving all steps from cell culture, stable isotope labeling (e.g. SILAC), sample preparation, LC-MSMS, and data analysis by various computational tools. This will be applied to one of the ongoing research projects, which is further explained here: http://www.dkfz.de/en/proteomik-stammzellen-krebs/index.php
36.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Daniel Lipka, Mark Hartmann d.lipka@dkfz.de 	 6-8 weeks; date to be arranged 9:00-18:00 DKFZ, TP4, INF 581 1-2 	Translational Cancer Epigenomics Epigenetic patterns enable the different cell types of our body to specifically interpret the information stored in our genome and provide situation-specific readouts. Epigenetic processes dynamically regulate cellular differentiation from embryonic development through to the adult organism, but they are also essential for homeostatic processes. In our group we investigate the epigenetic regulation of differentiation processes both in the normal and in the malignant context. We use in vivo and in vitro models as well as primary patient samples to study how genetic and epigenetic aberrations contribute to malignant transformation. Please refer to our website (www.translational-cancer-epigenomics.de) for further details. We offer internships in molecular and cellular biology, as well as projects in computational epigenomics, including single-cell epigenomics.
37.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Fabricio Loayza-Puch f.loayza-puch@dkfz.de 	 6-8 weeks; date to be arranged 9:00-18:00 DKFZ Main Building, INF 280, 2nd floor 1-2 	Uncovering metabolic vulnerabilities in cancer Cancers develop in very heterogeneous tissue environments. They depend on the tumor microenvironment (TME) for sustained growth, metastasis, and therapy resistance. The TME plays also a very important role as a source of nutrients for cancer cells. However, methods to study metabolic interactions in the TME are lacking. We recently harnessed ribosome profiling for sensing restrictive amino acids, and developed diricore, a procedure for differential ribosome measurements of codon reading. In this course, the student will join a project to develop and apply Dual Ribosome Profiling (DualRP), a system to study cell interactions in the TME. DualRP is an approach that allows not only simultaneous analysis of gene expression in two interacting cell populations in vivo, but also is able to uncover metabolic limitations in multiple cellular types in tumors by reading selectively the stalling of ribosomes.
38.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Justo Lorenzo Bermejo and co-workers lorenzo@imbi.uni- heidelberg.de 	 6-8 weeks; date to be arranged Full-time IMBI, INF 130.3, 12th floor, Rm 301 1-2 	Statistical analysis of molecular data: Applied bioinformatics with R The statistical analysis of genetic and molecular data plays today a major role in life sciences. A basic knowledge of biostatistics is essential for a successful academic career and many biotech/pharmaceutical companies are actively recruiting staff with an appropriate training. This internship aims to provide participants with an overview of standard methods, software and current developments in applied statistics for molecular medicine. After an introduction into the field including the R project for statistical computing, participants will gain hands-on experience in the R software. Previous programming experience is not required, but exposure to genetic-molecular data (DNA sequence, small-RNA or mRNA expression, methylation data, metabolomics, proteomics or microbiome data) is advantageous. The instructors are members of the Statistical Genetics Research Group at the Institute of Medical Biometry, Heidelberg University. Please visit <u>www.biometrie.uni-heidelberg.de/StatisticalGenetics</u> for a brief description of our research activities.

lfd Nr	Term	Туре	Supervisor(s)Contact	 Duration and date Time Location No. of places 	Title and Description
39.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) 	 Frank Lyko f.lyko@dkfz.de 	 to be arranged to be arranged TP3, INF 580 1-2 	Epigenetics The group is active in several areas of epigenetics research. Please refer to our website (<u>www.dkfz.de/epigenetics</u>) for further information. In addition to lab internships in molecular/cellular biology, the group also offers projects in computational biology, particularly single-cell sequencing data analysis.
40.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: Neuroscience, MCB, Dev. Biol.) 	 Ana Martin-Villalba, Susanne Kleber, and PhD students in the group a.martin-villalba@dkfz.de 	 to be arranged 10.00-18.00 TP4, INF 581, 3. OG BT I, 3.123 2-3 (one at a time) 	Neurogenesis in the young, old and diseased brain Stem cells Our lab is interested in the function and regulation of neural stem cells in the developing and adult brain. In the adult brain there are two regions harbouring neural stem/progenitor cells (NPCs) that continuously generate new neurons, the dentate gyrus of the hippocampus (DG) and the subventricular zone of the lateral ventricles (SVZ).Newborn neurons of the hippocampus are involved in learning and memory. Stem cells in the SVZ generate interneurons involved in fine tuning of olfaction. In the diseased brain, NPCs can be activated to repair the brain. Over- activation of these cells can result in tumour formation. To envisage ways to repair the CNS or block tumor formation the lab studies cell proliferation, and differentiation in the developing and healthy, tumorigenic, and regenerating adult CNS. Our laboratory has identified CD95 as a receptor signaling survival and neuronal differentiation in the naive and ischemic brain (Corsini et al., Cell Stem Cell 2009). Axonal regeneration Santiago Ramón y Cajal made several fundamental observations that have defined the perception of axonal regeneration in the central nervous system, regeneration of nerve fibers does occur, in the adult CNS they do not regenerate. Right after injury, transected axons in the brain and spinal cord extend short distances, but shortly afterwards regeneration is halted and growth cones turn into retraction bulbs (Cajal, 1928). Our laboratory tries to envisage new ways to coax axons towards regeneration using models of crush- and transection-injury of the spinal cord. <u>Signaling</u> CD95 was first described as the inducer of apoptosis and it is still mostly known as the "death receptor". However, research in our group questions this dogma. We showed in several cancer cell lines and primary cell types that CD95 does not act as an apoptosis inducer but rather triggers migration, invasion and differentiation. We have deciphered molecular events originating fro

lfd Nr	Term	Туре	Supervisor(s)Contact	 Duration and date Time Location No. of places 	Title and Description
41.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Milsom michael.milsom@dkfz.de 	 8 weeks lab-time full-time DKFZ, INF 280, H01.04.048 1 	Stem cells, DNA damage and ageing Cancer is one of several diseases whose incidence dramatically increases with advancing age. The Experimental Hematology group is broadly interested in understanding the mechanisms which govern this phenomenon and predominantly focusses upon the hematopoietic system as a model to study ageing. Specifically, we are interested in characterizing the biological changes that take place in hematopoietic stem cells during ageing and how these alterations impact upon hematopoietic function and the process of leukemogenesis.PLEASE NOTE: This Biolab rotation will involve working with experimental mice.For further details of the work program and associated literature, please visit https://www.dkfz.de/en/experimentelle-haematologie/index.phpNote:We also host long-term internships to guest and exchange students, please get in contact for individual arrangements.
42.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Michael Milsom michael.milsom@dkfz.de 	 starting January 2025 full-time DKFZ, INF 280, H01.04.048 1 	Deregulation of DNA damage response by Evi1 in acute myeloid leukemia Overexpression of the transcription factor Evi1 in acute myeloid leukemia (AML) correlates with poor prognosis and therapy resistance. This project employs in vitro and in vivo models to investigate Evi1's role in leukemogenesis and its deregulation of the DNA damage response. Utilizing multi-omics approaches and the dTAG system, we aim to elucidate the molecular mechanisms driven by Evi1. This will be investigated further in the context of Fanconi anemia, a disorder marked by defective DNA repair and a predisposition to AML. This project aims to identify and validate potential targets that might represent novel therapeutic windows. <u>References:</u> Birdwell et al., Blood Cancer Journal 2021; Lux et al., Hemasphere. 2023; Lopez et al., Blood 2023
43.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major: Infectious Diseases) and other interested students 	 Martin Müller martin.mueller@dkfz.de 	 to be arranged 9.00-18.00 ATV/IIC, INF242 1-2 	Viruses and cancer Projects from our group can be found under <u>http://www.dkfz.de/en/f035/</u> . We are interested in the development of a broadly cross-protective Papillomavirus vaccine which involves development of antigens and evaluation of humoral and cellular immune responses in particular the detection of neutralizing antibodies. In a second line of projects, we are studying mechanisms of cellular restriction for Adeno-associated virus vectors.

lfd Nr	Term	Туре	 Supervisor(s) Contact 	 Duration and date Time Location No. of places 	Title and Description
44.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: MCB, Infectious Diseases) and MSc Molecular Biotechnology 	 Dirk M. Nettelbeck, Guy Ungerechts d.nettelbeck@dkfz.de 	 to be arranged to be arranged DKFZ, ATV, 2.108 1 	Virotherapy: Engineering oncolytic adenoviruses and characterizing their modes of action Virotherapy is the treatment of cancer with so-called oncolytic viruses that selectively infect and kill cancer cells, followed by viral spread in the tumor and the induction of anti-tumor immunity. The Clinical Cooperation Unit "Virotherapy" (Head of division: Prof. Dr. Dr. Guy Ungerechts) explores new strategies for engineering effective oncolytic viruses and combination therapies (for more information, see https://www.dkfz.de/en/virotherapie/index.php). Our subgroup focuses on the engineering of oncolytic adenoviruses, which possess a DNA genome and a capsid without envelope. Besides screening of novel adenovirus serotypes for applications in virotherapy, we engineer adenoviruses aiming at tumor-specific infection, enhanced viral replication and/or tumor cell lysis, inducible gene expression and expression of therapeutic antibodies. In the practical, Master students will learn and apply selected techniques for genetic engineering of adenoviral genomes, production and purification of adenoviral particles, characterization of viral infectivity, viral replication, viral spread, host cell responses, the activation of immune responses and the expression and activity of therapeutic antibodies using cell cultures, primary cells and patient-derived models. Master students will work together with PhD students and postdocs. Specific contents of an internship will depend on on-going projects in the lab.
45.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) also for Master Molecular Biotechnology, Master Biochemistry) 	 Christiane Opitz, Tamara Prentzell, Pauline Pfänder c.opitz@dkfz.de t.prentzell@dkfz.de p.pfaender@dkfz.de 	 to be arranged full-time DKFZ, HH, INF 280, H2.01.034, H2.01.050 max. 2 at a time 	Metabolic Crosstalk in Cancer Metabolic crosstalk in cancer, amino acid metabolism, NAD metabolism, metabolic immune regulation, brain cancer, breast cancer, ovarian cancer
46.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) also for Master Molecular Biotechnology, Master Biochemistry) 	 Christiane Opitz, Ahmed Sadik c.opitz@dkfz.de a.sadik@dkfz.de 	 to be arranged full-time DKFZ, HH, INF 280, H2.01.034, H2.01.050 max. 2 at a time 	Computational analyses of metabolic crosstak in cancer
47.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) 	 Christoph Plass, Dieter Weichenhan, Ali Bakr, Ashish Goyal, Clarissa Gerhäuser, Maria Llamazares Prada, Michael Scherer c.plass@dkfz.de 	 to be arranged 8.00-18.00 DKFZ, HH, INF 280, 3. OG 1 	 Epigenetic profiling in cancer Epigenetic alterations contribute to tumorigenesis by deregulating cancer related genes. Our work focuses on several questions: What are the underlying mechanisms of epigenetic gene deregulation in cancer? What are the target genes for epigenetic deregulation and how does this deregulation occur? What is the function of such deregulated genes in normal tissue? Work in our group focuses on diverse leukemias and solid tumor malignancies including breast, prostate and lung cancer. We use various genome wide methods to profile DNA methylation (EPIC- and mouse arrays, WGBS, Oxford Nanopore) as well as various histone modifications and transcription factor binding (ACT-seq), genome-editing by CRISPR/Cas9), single-cell approaches (sn-RNA and ATAC-seq) and analyse chromatin conformation (4C assays). We offer both wet-lab as well as bioinformatic internships. For further information on specific ongoing projects please see also our web page at https://www.dkfz.de/en/CanEpi/

lfd Nr	Term	Туре	 Supervisor(s) Contact 	 Duration and date Time Location No. of places 	Title and Description
48.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major Neuroscience) and other interested students of biosciences 	 Stefan Pusch s.pusch@dkfz.de 	 to be arranged full-time DKFZ, HH, INF 280, H1.06.048-060 1-2 	Translational research on glioma The research focus of our Clinical Cooperation Unit Neuropathology (https://www.dkfz.de/de/neuropathologie/index.php) are brain tumors. We develop new diagnostics and are interested in translational research including drug development. A subgroup of brain tumors are the glioma, which are all considered incurable. My group at the DKFZ is especially interested in IDH-mutant glioma and glioblastoma. Our focus lies on deciphering the functional consequences of mutations and other alterations in these tumors, to find weakness, which can be exploited for new treatment options. We offer opportunities to participate on our work to elucidate the exact mechanism by which these tumors develop and how they behave under treatment. With this knowledge, we want to find new weaknesses of these tumors, which we could then translate into new therapeutic approaches. In our work, we apply standard molecular biology methods, cloning, biochemical methods, CRISPR/Cas9 and 3D cell culture from transgene mice and primary human cultures. To understand the changes in the cells, we apply different omics approaches (transcriptomics, methylomics, NGS, phospho-proteomics and proteomics). In more advanced projects, we also use different mouse models, to analyze the tumor in vivo.
49.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) also for Master Molecular Biotechnology, Master Biochemistry) and other interested students 	 Jens Puschhof jens.puschhof@dkfz.de 	 to be arranged full-time DKFZ, ATV, INF 242, A0.103 and ground/ first floor 1 	Dissecting bacteria-cancer communication using organoids and organ chip You will join a team of MSc and PhD students who are working together to understand how bacteria influence tumor behavior. For this, you'll work with our clinical partners to isolate and sequence bacteria directly from patient tumor samples. Based on these insights, you'll bring selected bacteria in contact with patient-derived organoids and organ chip models to understand how they can contribute to tumor behavior and develop strategies to interfere with these interactions. For all aspects of this project, you'll get detailed introductions into the techniques and concepts of cancer-microbiome interactions. You should enjoy teamwork and combining wetlab with analysis components of your MSc internship project! More info: <u>https://www.dkfz.de/en/mikrobiom-und-krebs/EMIL.html</u> <u>References:</u> Puschhof, Pleguezuelos-Manzano et al., Nature Protocols 2021 Pleguezuelos-Manzano, Puschhof, Huber et al., Nature 2020
50.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) also for Master Molecular Biotechnology) and other interested students 	 Michael Scherer michael.scherer@dkfz.de 	 to be arranged full-time DKFZ Main Building, INF 280 1 	Dissecting DNA methylation heterogeneity in tumors using computational solution and single-cell profiling DNA methylation is an important epigenetic modification, which has recently emerged as a biomarker for the classification of various cancer types including brain tumors and sarcomas. While in some subsets of tumors, bulk profiling generated clinically relevant insights, other tumor types such as Acute Myeloid Leukemia and Lung Cancer remain underexplored. This is largely due to the fact that tumors comprise a heterogeneous population of cells in which only a subset of cells carry a diagnostic of prognostic DNA methylation signal. During the projects that we propose in the research group 'Computational and Single-Cell Epigenomics', we will explore both computational solutions as well as single-cell technologies to investigate DNA methylation patterns in underexplored tumors. The students can select from a variety of research projects ranging from purely computational work until performing single-cell experiments. We are embedded in the Division of Cancer Epigenomics and thus interaction with both computational and experimental researchers is required. More information on the currently available projects can be found on our website: https://www.dkfz.de/en/CanEpi/comp.epi.html

lfd Nr	Term	Туре	Supervisor(s)Contact	 Duration and date Time Location No. of places 	Title and Description
51.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Marcel Schilling, Ursula Klingmüller m.schilling@dkfz.de 	 to be arranged to be arranged DKFZ, HH, INF 280, H1.05.040 1 	Analysis of information processing in by an integrative receptor and signaling-pathway model The hormone Erythropoietin (Epo) is the key regulator of erythropoiesis and regulates cell survival via the JAK2/STAT5 signaling pathway. We have recently demonstrated that information processing by EpoR and JAK2 at the plasma membrane is linear over a broad range of ligand concentrations and that the activation of STAT5 is directly linked to survival of erythroid progenitor cells. However, the mode of signal processing throughout the JAK2/STAT5 pathway remains elusive. The aim of this project is to combine these previously established models and calibrate the resulting mathematical model with quantitative data. Data generation will be performed by quantitative immunoblotting and qRT-PCR. Identifiability analysis of model parameters, model reduction and experimental design can be performed. Depending on the qualifications of the student, the focus of this lab practical will be on the experimental side, the modeling aspects or a combination of both methods. http://www.dkfz.de/en/systembiologie/index.php
52.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major Infectious Diseases) 	 Patrick Schmidt patrick.schmidt@nct- heidelberg.de 	 to be arranged full-time NCT, Floor 2 1 	Methods in adoptive immunotherapy In recent years, immunotherapy has become of great interest to researchers, clinicians and pharmaceutical companies, particularly in its promise to treat various forms of cancer. By activating a patient's own immune system, especially CAR T cell therapy achieved success in specifically eradicating tumor cells of hematologic malignancies. However, CAR T cells are sharp weapons that may overshoot or miss their target which often leads to life-threatening consequences. Thus, in order to offer a safe and efficient immunotherapy, CAR T cells need to be precisely controlled. We have developed AAV-based virus-like particles (AAVLPs) that structurally mimic the cellular target of a CAR. The specific CAR-AAVLP interaction leads to temporal unavailability of the CAR on the T cell surface which is directly linked to reduced cytotoxic activity of the T cell. Likewise, a control of undesired cross-reactivity of CAR T cells by designer AAVLPs could be anticipated for future use in cancer immunotherapy.
53.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Almut Schulze, Marteinn Snaebjörnsson, Felix Vogel, Lisa Schlicker almut.schulze@dkfz.de 	 to be arranged full-time TP4, INF 581 1 	Metabolic reprogramming in cancer Metabolic reprogramming is an emerging hallmark of cancer. Altered metabolic activity in cancer cells drives the production of macromolecules for rapid proliferation and allows cancer cells to survive under conditions of nutrient and oxygen deprivation that is frequently found in tumours. Moreover, metabolic processes contribute to the heterotypic interactions between cancer cells and the surrounding stroma to facilitate cancer progression and immune evasion. The overall aim of our work is to unravel how oncogenic signalling pathways interact with the metabolic network to drive essential biosynthetic pathways that promote cancer cell expansion. We monitor changes in metabolic gene expression and determine the transcriptional networks responsible for metabolic reprogramming in cancer. We also apply metabolomics using high-resolution LC/MS and metabolic flux analysis to determine alterations in metabolic activities of cancer cells. Moreover, we conduct targeted functional genetic screening to identify metabolic processes that are essential for the survival of cancer cells. A particular focus of our work are the sterol regulatory element binding proteins (SREBPs), a family of transcription factors that control the expression of enzymes involved in the synthesis of fatty acids and cholesterol. We are also interested in processes governing allosteric regulation of glycolysis and fatty acid synthesis and modification. References: Snaebjornsson, M. T., Janaki-Raman, S. & Schulze, A. Greasing the Wheels of the Cancer Machine: The Role of Lipid Metabolism in Cancer. Cell Metab 31, 62-76, doi:10.1016/j.cmet.2019.11.010 (2020). Schulze, A. & Harris, A. L. How cancer metabolism is tuned for proliferation and vulnerable to disruption. Nature 491, 364-373, doi:10.1038/nature11706 (2012).

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				LocationNo. of places	
54.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Major MCB) and other interested students, specifically Immunology or Molecular Medicine 	 Martina Seiffert m.seiffert@dkfz.de 	 to be arranged 9.00-18.00 TP3, 1.110 2 	Tumor immunology In this practical, students will gain knowledge in the field of tumor immunology and learn state- of-the-art laboratory techniques to study tumor-infiltrating immune cells. We will use patient- derived tumor samples (B cell lymphoma or brain metastases) as well as tumor mouse models. The immune cell content in these samples will be analysed and characterized by flow cytometry, immunohistochemistry or immunofluorescence stainings of tissue sections, and transcriptome analyses by RNA sequencing. We will further isolate cells of interest by magnetic- or fluorescence-activated cell sorting (MACS, FACS) and perform in vitro assays to determine their role and function in the tumor microenvironment. Coculture assays of immune cells and tumor cells will be further established to study the cross-talk of these cells and its pathological role. These studies aim at a better understanding of anti-tumor immune responses and especially of mechanisms that lead to tumor immune escape, including the development of myeloid-derived suppressor cells and exhausted effector T lymphocytes. Please see our website for more detailed information on ongoing projects: http://www.dkfz.de/en/genetics/pages/projects/CLL/CLL-en.html
55.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors in life biosciences) 	 Gianluca Sigismondo g.sigismondo@dkfz.de 	 to be arranged based on project Pathology Institute, INF 224, 4th floor, and DKFZ Main building, 6th floor 2 	Epigenetics of brain tumors investigated by mass spectrometry-based proteomics Liquid chromatography mass spectrometry (LC MS)-based proteomics represents the gold standard for the unbiased identification of proteins and their post translational modification (PTM) status. The prospective student will join the proteomic team of the Clinical Cooperation Unit of Neuropathology, and dissect the link between epigenetic deregulation, cancer predisposition, and targeted therapy. A particular focus will be on the protein phosphorylation status (i.e. phosphoproteome) and on the abundance of histone post translational modifications (hPTMs) in brain tumors. This information will be instrumental to better understand tumor biology, and to suggest high-effective epigenetic therapies. To achieve this goal, the student will adopt and optimize innovative low-input proteomics pipelines for the investigation of the different epigenetic layers from cell lines, fresh frozen and formalin fixed paraffine embedded tissues. In addition, the student will receive training and have hands-on experience on cutting-edge proteomic workflows encompassing sample preparation, mass spectrometry operation and MS data analysis.
56.	all-year offer collective heiCO # 8503WPM 100	 ▶ Biolab ▶ WiB (also for other Majors) 	 Aurelio Teleman a.teleman@dkfz.de 	 to be arranged full-time INF 580, TP3, B1.314 1 	Regulation of cell growth and metabolism in cancerWe are interested in studying the cancer signaling pathways that regulate cell growth and metabolism. To grow, cells need to synthesize all the necessary metabolic building blocks by activating the relevant metabolic pathways. We are interested to understand how an organism senses metabolite levels, either in diet or available to the cells, and how this affects cell physiology. We study both signaling pathways (such as insulin, PI3K and TOR) and metabolic pathways. The lab uses a wide range of techniques, from cell culture and biochemical approaches to in vivo genetics and organismal phenotyping. https://www.dkfz.de/en/signal-transduction-cancer/pages/research.html
57.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Sevin Turcan s.turcan@dkfz.de 	 to be arranged 9.00-18.00 INF 460 (NCT) Rm 02.1201-2 1 	Molecular basis of glioma development We are interested in understanding the molecular events that contribute to glioma development, recurrence and therapy resistance. Major ongoing efforts in our lab include investigating the epigenetic and genetic alterations unique to lower grade gliomas, characterizing the roles of deregulated transcription factors in glioblastoma, and defining epigenetic vulnerabilities of IDH mutant gliomas. For more information, please refer to our website: <u>https://www.klinikum.uni-heidelberg.de/Low- Grade-Gliomas.142000.0.html</u>

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58.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) also for BSc Biosciences also for BSc and MSc Molecular Biotechnology 	 Guy Ungerechts, Christine Engeland, Johannes Heidbüchel j.heidbuechel@dkfz- heidelberg.de 	 to be arranged to be arranged NCT, INF 460, 2. OG, 02.127 1 	Oncolytic Measles viruses for cancer therapy The Clinical Cooperation Unit "Virotherapy" is engineering and characterizing oncolytic Measles virus vectors for novel cancer therapies with the goal of translation toward clinical Phase I studies. Links: https://www.dkfz.de/en/virotherapie/index.php https://www.nct-heidelberg.de/en/the-nct/core-areas/medical- oncology/research/virotherapy.html
59.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: MCB, Infectious Diseases) also for MSc Molecular Biotechnology 	 Guy Ungerechts, Mathias F. Leber Mathias.Leber@nct- heidelberg.de 	 to be arranged to be arranged NCT, INF 460, 02.116 1 	Virotherapy: Genetic engineering, combining and characterization of viral cancer (immuno-)therapeutics Virotherapy is the treatment of cancer with so-called oncolytic viruses (OVs) that selectively infect and kill cancer cells, followed by viral spread in the tumor and the induction of anti-tumor immunity. The Clinical Cooperation Unit "Virotherapy" (Head of division: Prof. Dr. Dr. Guy Ungerechts) explores new strategies for engineering effective oncolytic viruses and combination therapies (for more information, see https://www.dkfz.de/en/virotherapie/index.php and https://www.nct-heidelberg.de/en/the-nct/core-areas/medical- oncology/research/virotherapy.html). Our subgroup focuses on genetic engineering of oncolytic (measles) viruses aiming at tumor-specific infection, enhanced replication, spread and/or tumor cell lysis, expression of therapeutic RNAs or proteins and multi-modal combination therapies (e.g., radio-/pharmaco-/immuno-virotherapy). Master students will learn and apply selected techniques for genetic engineering of OVs, production and propagation of viruses, characterization of infectivity, replication, spread, host cell responses, the activation of immune responses and the expression and activity of therapeutic RNAs/proteins using cell cultures, primary cells and/or patient-derived models. Specific contents of an internship will depend on on- going projects in the lab.
60.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for Majors: Systems Biology, Infectious Diseases and other interested students 	 Hedda Wardemann, Christian Busse t.pufall@dkfz.de 	 to be arranged 9.00-18.00 DKFZ, HH, INF 280, H2.06.077 2 	Molecular and functional adaptive immune receptor repertoire profiling Direct measurements of the composition of the antigen-receptor repertoire have long been limited due to the high degree of Immunoglobulin (Ig) and T cell receptor (TCR) gene diversity. To perform in-depth analyses of the B cell and T cell repertoires we have developed a platform for the high-throughput amplification and sequencing of Ig and TCR transcripts from single cells. The approach is fully compatible with the subsequent cloning and expression of recombinant monoclonal antibodies and TCRs. Our lab combines experimental tools and assays (e.g. PCR, cloning, cell assays, Western Blot, ELISA) with bioinformatics/computational methods (e.g. sequence analysis) to analyze Ig and TCR repertoires at single-cell level in mice and humans. We are offering one experimental and one computational placement. The experimental project will include the application of two to three different methods as well as the analysis and presentation of the results. In the computational project we would like to focus on the clonal composition and evolution of B cell populations. Therefore, this placement requires intermediate-level proficiency of a programming language (preferred: R, Python, Perl). Previous experience with SQL databases and/or Linux systems is an advantage. For further details see: <u>https://www.dkfz.de/en/b-zell-immunologie/</u>

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61.	all-year offer collective heiCO # 8503WPM 100	Biolab WiB (also for other Majors)	Tim Waterboer t.waterboer@dkfz.de	 No. of places 6-8 weeks; date to be arranged full-time DKFZ, ATV 1 	Infections and cancer epidemiology The "Infections and Cancer Epidemiology" group deals with cancers caused by infections with e.g. Human Papillomaviruses (HPV), <i>Helicobacter pylori</i> , or Epstein-Barr virus (EBV). Our main aim is to discover novel serological biomarkers for diagnosis and early disease detection, and as progression markers. To this end, we develop high-throughput multiplexed serological methods and whole proteome microarrays. In combination with epidemiological methods, we perform a cross-discipline research approach involving lab-based assay development_data-driven research_and clinical application
62.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Frank Westermann, Umut Toprak, Sina Kreth, Kai-Oliver Henrich f.westermann@dkfz.de 	 to be arranged full-time DKFZ, HH, INF 280 3 	https://www.dkfz.de/en/infections-cancer-epidemiology/index.php Biolab internships in the Division of Neuroblastoma Genomics We offer projects in five topics that are the main research areas of the lab. • Topic 1: The Cell Cycle Clock • Topic 2: MYC Oncoproteins • Topic 3: Telomere Biology • Topic 5: Bioinformatics in Cancer Research In all projects experimental work is combined with high-throughput data analysis. We have a strong experimental focus on epigenetic and single cell analysis.
63.	all-year offer collective heiCO # 8503WPM 100	 Biolab WiB (also for other Majors) and other interested students 	 Stefan Wiemann s.wiemann@dkfz.de 	 to be arranged 9.00-18.00 DKFZ, TP3, INF 580 1-2 	Communication of tumor and stromal cells aiding resistance development Chemotherapy is the standard of care in the treatment of many aggressive tumor diseases, including breast cancer. Many tumors show an initial good response to chemotherapy, however, resistance often manifests. Tumor physiology and response to therapy are orchestrated by an intricate interplay between47 cancer and stromal cells collectively forming the tumor microenvironment. Several tumor cell-intrinsic resistance mechanisms have been discovered, however, the impact of the tumor stroma on therapy resistance has not been studied extensively. Carcinoma-associated fibroblasts (CAFs) are a major component of the stroma and secrete ECM components, growth factors, cytokines, proteases and hormones, suggesting their strong involvement in tumor initiation and progression. We have previously shown that paracrine signaling from chemotherapy-treated cancer cells to stromal fibroblasts can drive cancer cell recovery after cytotoxic drug withdrawal. In the practical, molecular and cell biology techniques will be applied to better understand the cross-talk between tumor cells and primary fibroblasts. Literature: https://www.ncbi.nlm.nih.gov/pubmed/33476079, https://www.ncbi.nlm.nih.gov/pubmed/33692466